Complete Summary

GUIDELINE TITLE

Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 32 p. (Technology appraisal guidance; no. 138).

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic asthma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Internal Medicine
Pediatrics
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of inhaled corticosteroids used alone or in combination with long-acting beta-2 agonists for the treatment of chronic asthma

TARGET POPULATION

Adults and children aged 12 years and older with chronic asthma

INTERVENTIONS AND PRACTICES CONSIDERED

1. Inhaled corticosteroid (ICS)
2. A combination of ICS and long-acting beta-2 agonist (LABA) using either a combination device or separate devices for each agent

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Objective measures of lung function (e.g., forced expiratory volume in the first second [FEV_1], peak expiratory flow rate [PEFR])
    - Symptoms (e.g., symptom-free days and nights)
    - Incidence of mild and severe acute exacerbations
    - Use of systemic corticosteroids
    - Adverse effects of treatment
    - Health related quality of life
    - Mortality
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG), Peninsula Medical School and Southampton Health Technology Assessments Centre (SHTAC), University of Southampton. (See the "Availability of Companion Documents" field.)

Clinical Effectiveness

Identification of Studies

A search strategy for electronic bibliographic databases was devised and tested by an experienced information scientist (refer to Appendix 3 of the Assessment Report [see the "Availability of Companion Documents" field]). Once finalised it was applied to a number of databases including: The Cochrane Database of Systematic Reviews (CDSR); The Cochrane Central Register of Controlled Trials; Database of Abstracts of Reviews of Effectiveness (DARE); the National Health Service Economic Evaluation Database (NHS EED); Medline (Ovid); Embase (Ovid); National Research Register; Current Controlled Trials; Institute for Scientific Information (ISI) Proceedings (Web of Knowledge); Science Citation Index (Web of Knowledge); and BIOSIS.

Searches were run up to February/March 2006, and were restricted to studies published in English. An update search was conducted in October 2006.

The drug manufacturers' submissions to NICE, which were received in August 2006, were also searched for potentially relevant trials.

Additional searches of MEDLINE, EMBASE, the Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment (HTA) Database and Cochrane Database of Systematic Reviews were conducted to identify systematic reviews of the long-term adverse events associated with either inhaled corticosteroid (ICS) use alone or in combination with a long-acting beta-2 agonist (LABA). For a copy of the full search strategy and search dates refer to Appendix 3 of the Assessment Report (see the "Availability of Companion Documents" field).

All identified studies were downloaded into a Reference Manager database for storage and retrieval as necessary. A keywording system was devised to enable each reference to be categorised according to pre-specified inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were specified *a priori* based on the scope issued by NICE as agreed in the published protocol.

Intervention

Trials reporting evaluations of the following ICS were included:

- Beclometasone dipropionate (BDP)
- Budesonide (BUD)
- Ciclesonide (CIC)
- Fluticasone propionate (FP)
- Mometasone furoate (MF)

Trials reporting evaluations of the following ICS combined with LABAs in the same inhaler (i.e., combination inhalers) were included:

- BUD/formoterol fumarate (FF)
- FP/salmeterol (SAL)

Trials reporting ICS delivered by pressurised metered-dose inhaler (pMDIs) (chlorofluorocarbon [CFC] and hydrofluoroalkane [HFA] excipients), and by dry powder inhalers (DPIs) were included, however, those using nebulisers were excluded.

To be included the treatment had to last for greater than four weeks.

Comparators

- The ICS were compared with each other.
- The combination inhalers were compared with: each other; and with ICS only. They were also compared with ICS and LABAs administered in separate inhalers.
- Trials testing only different doses of the same agent were not included as these were outside the scope of the assessment. However, trials which compared more than one dose of an ICS against a different ICS were included.
- Trials testing different ICS by different inhalers or propellants were not included (e.g., DPI versus pMDI, or HFA pMDI versus CFC pMDI).
- NB. Trials reporting comparisons between ICS and placebo were sought and included in order to potentially support economic modelling (e.g., model parameters). Details of these studies are not reported in the assessment of clinical effectiveness.

Types of Studies

- Fully published randomised controlled trials (RCTs) or systematic reviews of RCTs. Double blinding was not a pre-requisite for inclusion, although blinding was assessed as part of critical appraisal. Indicators of a 'systematic' review include: explicit search strategy, inclusion criteria, data extraction and assessment of quality.
- Trials reported in abstracts or conference presentations from 2004 onwards were retrieved, however their details were not extracted, critically appraised or analysed (NB. the exception to this was where an abstract was available which provided data supplementary to a fully published trial report of a particular study. This occurred in a handful of cases).

- Where unpublished full trial reports were available (e.g., as supplied by the drug manufacturers in their submissions to NICE) these were included.

Population

- Adults and children aged 12 years and over diagnosed with chronic asthma. Studies in which the patient groups were asthmatics with a specific related co-morbidity (e.g., bronchitis; cystic fibrosis) were not included, except for chronic obstructive pulmonary disease (COPD) as requested in the NICE Scope.
- Studies reporting the treatment of acute exacerbations of asthma were not included.
- Trials reporting the effectiveness of ICS with LABAs were only included if the patients had been previously treated with an ICS.

Outcomes

At the inclusion/exclusion screening stage studies reporting one or more of the following outcomes were included:

- Objective measures of lung function (e.g., forced expiratory volume in one second [FEV_1], peak expiratory flow rate [PEFR])
- Symptoms (e.g., symptom-free days and nights)
- Incidence of mild and severe acute exacerbations (e.g., mild – requiring unscheduled contact with healthcare professional; severe – requiring hospitalisation, systemic corticosteroids or visit to accident and emergency department)
- Use of systemic corticosteroids (e.g., prednisolone)
- Adverse effects of treatment
- Health-related quality of life
- Mortality

Titles and abstracts of studies identified by the searches were screened by one reviewer based on the above inclusion/exclusion criteria. A second reviewer checked a random 10% of these. Any discrepancies were resolved through discussion and involvement of a third reviewer where necessary.

Full papers of studies included on title or abstract were requested for further assessment. All full papers were screened independently by one reviewer and checked by a second. Any discrepancies were resolved by discussion with involvement of a third reviewer where necessary.

All included papers were keyworded in the Reference Manager database as to their intervention and comparator, and were coded for the synthesis framework to enable efficient retrieval of sub-sets of studies for analysis.

As far as possible all included papers describing a particular trial were linked together to form a 'set' of studies. One of the papers (usually the seminal journal article reporting the key efficacy and safety results) was designated as the primary publication, with the remaining papers classed as secondary publications.

All included trials were cross-referenced with the relevant Cochrane reviews to ascertain whether or not they had already been included in the reviews. Those that were included were keyworded in the Reference Manager database accordingly. Conversely, the bibliography of included studies in the relevant Cochrane reviews were cross-referenced with the list of included studies and the inclusion criteria to ascertain whether there were any relevant studies in those reviews that had not been identified by the ERG search.

Cost-Effectiveness

Search Strategy and Critical Appraisal Methods

Ten electronic databases including MEDLINE, EMBASE and the Cochrane Library (Issue 1, 2006) were searched for cost-effectiveness studies that assessed the cost-effectiveness of BDP, BUD, FP dipropionate, CIC and MF used alone or in combination with a LABA (SAL or FF) within their licensed indications and the appropriate step of the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) Guidelines. The full search strategy is shown in Appendix 3 of the Assessment Report (see the "Availability of Companion Documents" field). The original searches were conducted in April 2006 with updated searches in October 2006.

Inclusion and Exclusion Criteria

Full, published cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost-consequence analyses were eligible for inclusion in the cost-effectiveness review.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

A total of 113 records describing 84 studies were included. Of the 84 studies:

- 10 were conference abstracts published from 2004 onwards
- 7 were systematic reviews (of which 5 were Cochrane reviews)
- 67 were randomised controlled trials (RCTs) (of which 38 had been included in the Cochrane reviews)

Cost-Effectiveness

- Fifteen published economic evaluations met the inclusion criteria
- Six reports were provided by manufacturers

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Peninsula Technology Assessment Group (PenTAG), Peninsula Medical School and Southampton Health Technology Assessments Centre (SHTAC), University of Southampton. (See the "Availability of Companion Documents" field.)

Clinical Effectiveness

Data Extraction Strategy

All trials, except those included in the relevant Cochrane reviews, were fully data extracted. Data were entered into a structured template by one reviewer and checked by a second. Any discrepancies between the data extracted and the original trial report were resolved and the data extraction was finalised.

Critical Appraisal Strategy

The methodological quality of the trials supplemental to the Cochrane reviews was assessed according to criteria specified by the Centre for Reviews and Dissemination (CRD). (Refer to Appendix 4 of the Assessment Report [see the "Availability of Companion Documents" field]). Quality was assessed by one reviewer and their judgements were checked by a second. Where there was disagreement a third reviewer was consulted and a final judgement agreed.

Methods of Data Synthesis

Results of the included trials were synthesised narratively with use of meta-analyses where possible and where appropriate. A framework was devised for the analysis and presentation of results, based on the step wise approach recommended in the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) Guidelines for the management of asthma.

The review questions were:

1. Which inhaled corticosteroid (ICS) is the most-effective at low doses (200–800 micrograms per day beclometasone dipropionate/budesonide [BDP/BUD] equivalent) (Step 2 of the guidelines)

2. Which ICS is the most-effective at high doses (800–2000 micrograms per day BDP/BUD equivalent) (Step 4 of the guidelines)
3. Which is the more clinically effective approach to introducing a long-acting beta-2 agonist (LABA) into a treatment regimen:
    - To increase the dose of ICS alone or to add a LABA to treatment with ICS using a combination inhaler? (Steps 2-3 of the guidelines)
    - To continue with an ICS alone or to add a LABA to treatment with a similar dose of ICS using a combination inhaler? (Steps 2-3 of the guidelines)
4. Which is the more clinically effective treatment: fluticasone propionate (FP) and salmeterol (SAL) in a combination inhaler or given in separate inhalers? BUD and formoterol fumarate (FF) in a combination inhaler or given in separate inhalers?
5. Which is the most-effective—a combination inhaler containing BUD/FF, or a combination inhaler containing FP/SAL? (Step 3 of the guidelines)

Each included trial was coded according to which of the review questions it was relevant to. Some trials were relevant to more than one review question as they tested multiple doses of inhaled steroids.

Each review question was stratified according to a number of pair-wise comparisons of the inhaled steroids and, where relevant, LABAs (where evidence allows). In addition, some trials were included in more than one pair-wise comparison as they evaluated two or more ICS (e.g., a three arm trial comparing FP with BUD and BDP).

Trials were also divided according to whether or not a parallel-group or cross-over design was used. It is generally considered inappropriate to pool these designs together within a meta-analyses. Where necessary trials were then further divided according to the nominal dose ratio employed, following the approach used in the Cochrane review of FP compared to BUD or BDP.

In summary, the framework comprised sets of trials grouped according to which review question, pair-wise comparison, study design, and dose ratio they related to.

Narrative Synthesis

Within each pair-wise comparison all included trials were tabulated for their key characteristics and described in the text (e.g., trial duration, patient profile, outcome measures, methodological quality). In addition, more detailed data on the trials are available in Appendix 4 of the Assessment Report (see the "Availability of Companion Documents" field), for those trials which were supplemental to the Cochrane reviews (and which underwent full data extraction).

Meta-Analysis

The feasibility and appropriateness of meta-analysis was considered once narrative syntheses had been completed. The decision to pool was mediated by the likelihood that the trials were clinically homogenous, and that the necessary data were available. Potential clinical heterogeneity was assumed if there were differences between trials in:

- Dose
- Disease severity
- Treatment duration

If pooling was considered appropriate the data in each trial were examined to ascertain whether or not sufficient details were reported to facilitate meta-analysis. The Cochrane Airways Group kindly supplied their Review Manager software files containing extracted and analysed data. These files were edited to correspond to the Assessment Group's review questions and framework (i.e., they were assembled into smaller sets of studies based on dose, design, and pair-wise comparisons). Data from trials included in the Cochrane reviews which did not meet the inclusion criteria for this review were removed. Data from trials supplemental to the Cochrane reviews were added, based on the data extracted to our standardised template.

For continuous outcome measures (e.g., lung function, symptoms) mean values and standard deviations were required in order to calculate mean differences. These were entered where available from the trial reports. Where standard deviations were not reported they were converted from standard errors, *p* values, or confidence intervals provided in the trial reports (where available), using standard formulae within a spreadsheet. Authors were not contacted to supply missing data.

Cross-over trials were only pooled where data were reported to facilitate appropriate analysis. Many cross-over trials report results as if the trial used a parallel-group design and pooling is not advised, as this results in a unit of analysis error. In such cases cross-over trials were described narratively, with appropriate caveats.

Pooled data were expressed separately in terms of change from baseline to end-point, and as end-point values. Trials were pooled within a meta-analysis as either one of these, but not both. The Assessment Group chose not to impute change values where not reported by authors as it requires estimations of the variance around mean differences, which involves assumptions about within-patient differences. Data were not available to allow within-patient differences to be estimated (e.g., from an appropriate correlation co-efficient).

Much of the data were continuous and where it was apparent that the same measurement scale had been used across studies a weighted mean difference (WMD) was used to summarise treatment effects. If it appeared that different measurement scales were employed a standardised mean difference (SMD) was used. Dichotomous data (e.g., rate of adverse events) were pooled using odds ratios. 95% confidence intervals were used for all measures of effect. A fixed-effects model was used, with random-effects model used if statistical heterogeneity was apparent. Statistical heterogeneity was measured using a chi-squared test with $p<0.10$ as the level of significance. The I^2 statistic was also used, whereby a value in excess of 50% indicates substantial heterogeneity.

Refer to sections 5.1.3 to 5.1.5 of the Assessment Report (see the "Availability of Companion Documents" field) for more information.

Cost-Effectiveness

Refer to Section 6.5 in the Assessment Report (see the "Availability of Companion Documents" field) for information about the methods used in the original economic analysis.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Assessment Group conducted a systematic review of published economic evaluations of asthma and identified 15 studies. Four studies were analysed from the United Kingdom National Health Service (UK NHS) perspective but only one calculated an incremental cost per quality-adjusted life year (QALY). This analysis produced incremental cost-effectiveness ratios (ICERs) of 4800 to 18,300 pounds sterling per QALY gained for fluticasone propionate/salmeterol compared with fluticasone propionate alone at various dose levels. However, the analysis pooled effectiveness and resource-use data from patients in 44 countries and, for this reason, the Assessment Group concluded that the generalisability of these results to the UK setting may be limited.

Seven submissions were produced by six manufacturers (Altana, AstraZeneca, GlaxoSmithKline, IVAX, Meda and Trinity Cheisi). There was no submission from the manufacturer of mometasone furoate (Schering-Plough). All manufacturers produced a cost-minimisation analysis for the inhaled corticosteroid (ICS) products but none of the submissions compared all five available ICSs. Four submissions focused on either the device or the propellant associated with the ICS and one on the ICS itself. Two submissions produced a cost-effectiveness analysis for the combination devices from a product-specific perspective.

The Assessment Group addressed the economic evaluation of the five questions addressed in the effectiveness section (see section 4.1.2 of the original guideline document). Two of the questions relate to the comparison of ICSs as monotherapy at low and high doses, while three address the use of combination therapy (adding a long-acting beta 2 agonist [LABA] to inhaled corticosteroid [ICS] treatment compared with increasing the dose of ICS; treatment with separate devices compared with a combination device; and comparing the available combination devices). Where consistent evidence of differential clinical effectiveness was lacking, a cost-minimisation approach was used. If there was relatively consistent evidence showing differential effectiveness, a cost-consequence approach was adopted.

When the cost of taking a combination device is compared with taking the components separately, the combination product is almost always cheaper than taking the same drugs in separate devices. For the budesonide/formoterol fumarate combination, annual savings vary from 36 pounds sterling to 227 pounds sterling depending on the daily dose of ICS and the preparation of the LABA used. For the fluticasone propionate/salmeterol combination the annual savings vary from 39 pounds sterling to 185 pounds sterling.

At the lower dose level (400 micrograms budesonide and 200 micrograms fluticasone propionate daily, given as regular twice-daily doses), the cheapest combination device is the fluticasone propionate/salmeterol aerosol pressurized metered dose inhaler (pMDI), which costs 219 pounds sterling per year and is only 12 pounds sterling cheaper than the budesonide/formoterol fumarate dry powder inhaler (DPI). The annual cost of low dose fluticasone propionate/salmeterol delivered by DPI (379 pounds sterling) is 148 pounds sterling more costly than budesonide/formoterol fumarate DPI (231 pounds sterling). At the higher dose level (800 micrograms budesonide and 500 micrograms fluticasone propionate), the fluticasone propionate/salmeterol DPI and pMDI are the cheapest at 446 pounds sterling per year, which is 16 pounds sterling cheaper than the budesonide/formoterol fumarate DPI.

See section 4.2 in the original guideline document for further discussion of the cost analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The future discontinuation of chlorofluorocarbon (CFC)-containing inhalers will affect the range of devices available, but does not affect this guidance.

For adults and children aged 12 years and older with chronic asthma in whom treatment with an inhaled corticosteroid (ICS) is considered appropriate, the least costly product that is suitable for an individual, within its marketing authorisation, is recommended.

For adults and children aged 12 years and older with chronic asthma in whom treatment with an ICS and long-acting beta-2 agonist (LABA) is considered appropriate, the following apply.

- The use of a combination device within its marketing authorisation is recommended as an option.
- The decision to use a combination device or the two agents in separate devices should be made on an individual basis, taking into consideration therapeutic need and the likelihood of treatment adherence.
- If a combination device is chosen then the least costly device that is suitable for the individual is recommended.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of inhaled corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and older

POTENTIAL HARMS

The side effects of inhaled corticosteroids (ICSs) may be local (following deposition in the upper airways) or systemic (following absorption into the bloodstream).

- Local adverse effects include dysphonia, oropharyngeal candidiasis, cough, throat irritation and reflex bronchospasm. Local adverse effects can be minimised by optimising inhaler technique and using a spacer with the inhaler device.
- Systemic adverse effects include suppression of the hypothalamic-pituitary-adrenal axis, osteoporosis, skin thinning and easy bruising, cataract formation and glaucoma, and growth retardation in children and adolescents. Systemic adverse effects tend to be associated with higher doses of corticosteroids and can differ depending on both the drug and the delivery system.

For full details of side effects and contraindications, see the summaries of product characteristics available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Limitations of the Systematic Review of Clinical Effectiveness

- It was not possible to report every outcome measure reported in each of the included trials. There are numerous ways of measuring and reporting measures of asthma control. To achieve brevity the Assessment Group prioritised key measures from each of the relevant outcomes.
- It was not always possible to conduct meta-analysis in order to provide a quantitative estimate of treatment effect. This would have provided greater statistical power to show differences. Differences between studies in length and dose meant that in many instances it was not appropriate to pool studies. In cases where pooling was appropriate poor reporting of the results of the trials prohibited quantitative synthesis (e.g., limited data available on the variance associated with effect measures). Consequently, much of the assessment of clinical effectiveness has been reported narratively. It has been challenging summarizing such a large evidence base in this way.
- The quality of reporting in the trial reports was poor in places. For example, the brand name for the inhaled steroids and the devices used to dispense them were not always mentioned. It was also particularly difficult to determine whether or not a combination inhaler had been used, or whether inhaled corticosteroid (ICS) and long-acting beta-2 agonist (LABA) had been delivered by separate inhalers.

Limitations of the Economic Evidence and Analyses

- The main limitation of the economic analyses is that they do not include a comprehensive model-based cost-utility analysis which integrates all relevant cost and effectiveness evidence relevant to the decision problems. This omission is partly due to the nature of the published trial evidence base for these decision problems, but also to do with the inherent challenges of modelling the full spectrum of asthma outcomes, from symptom control and quality of life impacts to severe exacerbations.
- All of the cost comparisons discussed above have involved a number of necessary simplifying assumptions including 1) the relative doses of different ICS drugs which are currently assumed to have equivalent effectiveness, 2) the exact mix of products which would probably be used to achieve any particular daily dose level of ICS or ICS-with-LABA, and 3) using 2005 community prescription sales as a way of producing a weighted mean annual

cost for each group of drug preparations. For these reasons, and because the range of available ICS and combination products is currently undergoing considerable change (with chlorofluorocarbon [CFC]-containing products being phased out, and some new hydrofluoroalkane [HFA]-propelled beclometasone dipropionate [BDP] products recently entering the market), the conclusions should be viewed with appropriate and substantial caution.

Refer to sections 8.5.1 and 8.5.2 of the ERG Report (see the "Availability of Companion Documents" field) for additional information on limitations of clinical effectiveness and cost-effectiveness analyses.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE Web site (www.nice.org.uk/TA138; see also the "Availability of Companion Documents" field).
    - Audit support for monitoring local practice.
    - A costing statement explaining the resource impact of this guidance.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 32 p. (Technology appraisal guidance; no. 138).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Mar

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Professor AE Ades, MRC Senior Scientist, MRC Health Services Research Collaboration, Department of Social Medicine, University of Bristol; Anne Allison, Nurse Clinical Adviser, Healthcare Commission; Dr Tom Aslan, General

Practitioner, Stockwell, London; Professor David Barnett *(Chair)* Professor of Clinical Pharmacology, University of Leicester; Mrs Elizabeth Brain, Lay Member; Dr Karl Claxton, Health Economist, University of York; Dr Richard Cookson, Senior Lecturer in Health Economics, School of Medicine Health Policy and Practice, University of East Anglia; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Professor Christopher Eccleston, Director, Pain Management Unit, University of Bath; Dr Paul Ewings, Statistician, Taunton and Somerset NHS Trust, Taunton; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Director of Finance, Barts and the London NHS Trust; Mr Adrian Griffin, Health Outcomes Manager, Johnson & Johnson Medical Ltd; Ms Linda Hands, Clinical Reader in Surgery, University of Oxford; Dr Rowan Hillson, Consultant Physician, Diabeticare, The Hillingdon Hospital; Professor Philip Home *(Vice Chair)* Professor of Diabetes Medicine, University of Newcastle upon Tyne; Dr Terry John, General Practitioner, The Firs, London; Professor Richard Lilford, Professor of Clinical Epidemiology, Department of Public Health and Epidemiology, University of Birmingham; Dr Simon Maxwell, Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queens Medical Research Institute, University of Edinburgh; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Ms Judith Paget, Chief Executive, Caerphilly Local Health Board, Wales; Dr Ann Richardson, Lay Member; Mr Mike Spencer, General Manager, Clinical Support Services, Cardiff and Vale NHS Trust; Dr Simon Thomas, Consultant Physician, General Medicine and Clinical Pharmacology, Newcastle Hospitals NHS Trust; Mr David Thomson, Lay Member; Dr Norman Vetter, Reader, Department of Epidemiology, Statistics and Public Health, School of Medicine, Cardiff University, Cardiff; Dr Paul Watson, Director of Commissioning, East of England Strategic Health Authority

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 2 p.

(Technology appraisal 138). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

- Costing statement: inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 4 p. (Technology appraisal 138). Available in Portable Document Format (PDF) from the NICE Web site.
- Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 7 p. (Technology appraisal 138). Available in Portable Document Format (PDF) from the NICE Web site.
- ICS and LABAs for the treatment of chronic asthma in adults and children aged 12 years and over: systematic review and economic analysis. Assessment report. 2006 Dec 20. 665 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1495. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Inhaled corticosteroids for the treatment of chronic asthma in adults and in children aged 12 years and over. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Mar. 4 p. (Technology appraisal 138).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1496. 11 Strand, London, WC2N 5HR.

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